

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NEW YORK UNIVERSITY]

The Reaction of Bisulfite with Epoxy Compounds

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The addition of sulfurous acid salts to the oxirane ring has been found to proceed by an ionic mechanism. The ionic species directly involved is sulfite ion. For epoxides of limited water solubility, the reaction is first order with respect to sulfite ion concentration. Additions to alkyl and aryl epoxides result in the formation of hydroxy secondary sulfonic acids as the chief products. A phenoxymethyl group adjacent to the oxirane ring reverses the direction of addition, with the production of hydroxy primary sulfonic acids. Similar behavior has been observed in the oxetane system. At lower *pH*'s the chief reaction here is rearrangement, with the formation of an aldehyde addition compound.

It has been known for many years that salts of sulfurous acid will add to epoxides. This reaction was first observed in 1868 by Erlenmeyer and Darmstaedter,² who found that sodium isethionate was formed when ethylene oxide and a solution of sodium bisulfite were heated in a sealed tube at 100°. Numerous further examples of this reaction have since been reported.³⁻⁶

It has been shown by Kharasch and his co-workers^{7,8} that, except for additions to double bonds conjugated with carbonyl or nitrile linkages,⁹ the reaction of bisulfite with an olefinic double bond involves an intermediate free radical generated by the action of an oxidizing agent on sulfite or bisulfite ion. The many similarities in behavior of oxirane rings and olefinic double bonds indicate a certain structural relationship, which in turn suggests a possibility that the addition of bisulfite to epoxides might proceed by a free-radical mechanism. The problem has been attacked in two ways: by studying the effect of oxidizing agents on the reaction and by determining the orientation of the addition products.

In the study of the effect of oxidizing agents on the addition of bisulfite to the oxirane system, bisulfite free radicals were generated in the presence of the epoxides by vigorously shaking mixtures of epoxide and one molar aqueous sodium bisulfite in an atmosphere containing oxygen. In an alternative procedure, oxygen was excluded and sodium nitrite was used as the oxidant. When the absence of oxidizing agents was desired, the reactions were carried out *in vacuo*. Hydroquinone or *t*-butylcatechol was included in several experiments under high vacuum to ensure the complete inhibition of any potential peroxide-catalyzed addition. The results of four representative additions to styrene oxide are given in Table I. Since it has been shown by Kharasch, *et al.*,^{7,8} that the peroxide-catalyzed addition of bisulfite to olefins proceeds with maximum efficiency in the vicinity of *pH* 6, several reactions were carried out in which the bisulfite solu-

tion was buffered by the presence of sodium sulfite. The results of these additions are summarized in Table II. It was quickly apparent that the presence of an oxidizing agent was not essential to the addition. In fact, the amount of sulfurous acid salts which added was greater in those runs where oxidizing agents were excluded. It is therefore concluded that the addition does not proceed *via* a free-radical mechanism.

TABLE I

THE EFFECT OF OXIDANT CONCENTRATION ON THE ADDITION OF NaHSO₃ TO STYRENE OXIDE^a

Oxygen tension, mm.	Initial <i>pH</i>	Final	Time, hours ^b	SO ₃ converted to addition product, %
152	4.35	3.2	3	6
10 ^{-4c}	4.35	4.4	6	11
10 ⁻⁴	4.35	4.4	6	11
<i>d</i>	4.35	3.4	3	4

^a The initial concentration of sodium bisulfite was approximately one molar in all cases. ^b In every case, the reaction was permitted to continue until sodium bisulfite was no longer consumed. ^c Hydroquinone added; 0.01 mole per mole of sodium bisulfite. ^d Oxygen absent; 0.05 mole of sodium nitrite per mole of sodium bisulfite, introduced at one time.

TABLE II

THE EFFECT OF OXIDANT CONCENTRATION ON THE ADDITION OF SULFUROUS ACID SALTS TO STYRENE OXIDE^a

Oxygen tension, mm.	Initial <i>pH</i>	Final	Time, hours ^b	SO ₃ converted to addition product, %
152	6.15	6.3	3.5	30
5 × 10 ⁻⁴	6.15	>13	6	74
10 ^{-4c}	6.15	>13	6	74

^a The total initial concentration of sulfurous acid salts in solution was approximately one molar in all cases; the molar ratio of sodium bisulfite to sodium sulfite was 60:40. ^b In every case, the reaction was permitted to continue until sulfurous acid salts were no longer consumed. ^c *t*-Butylcatechol added; 0.01 mole per mole of sulfurous acid salts.

Where the sodium bisulfite solutions were buffered with sodium sulfite, the rate at which sulfurous acid salts were consumed was greatly increased. It was also noticed that in several runs the solutions became strongly alkaline. Additional experiments were carried out to determine the effect of the initial *pH* of the bisulfite-sulfite solution on the rate of addition of sulfurous acid salts to styrene oxide. These were conducted in the absence of oxidizing agents. The results are summarized in Table III. It is obvious that the higher the concentration of sulfite ion in solution, the greater the rate of the

(1) This paper is based on the thesis submitted by Samuel Kaizerman to the Graduate Faculty of New York University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) E. Erlenmeyer and L. Darmstaedter, *Z. Chem.*, 342 (1868).

(3) L. Darmstaedter, *Ann.*, **148**, 125 (1868).

(4) F. O. Pazsche, *J. prakt. Chem.*, [2] **1**, 86 (1870).

(5) L. Brunel, *Compt. rend.*, **137**, 63 (1903).

(6) German Patent 569,148 (1931).

(7) M. S. Kharasch, E. M. Mayo and F. R. Mayo, *Chemistry and Industry*, **57**, 774 (1938).

(8) M. S. Kharasch, R. T. E. Schenck and F. R. Mayo, *THIS JOURNAL*, **61**, 3092 (1939).

(9) R. T. E. Schenck and I. Danishefsky, *J. Org. Chem.*, **16**, 1683 (1951).

addition. This indicates that sulfite rather than bisulfite is the reacting species.

The product of the addition of sulfite to styrene oxide was shown to be sodium 1-phenyl-2-hydroxyethane sulfonate by comparison with a known sample prepared by unambiguous synthesis. No other addition product could be isolated. Similar studies were conducted on other epoxides, in order to determine the effect on the direction and course of the addition of replacing the phenyl group in styrene oxide by other substituents. The only product which could be obtained from the reaction with 1,2-epoxyoctane was sodium 1-hydroxyoctane-2-sulfonate; the influence of a *n*-hexyl group is thus comparable to that of phenyl, though the somewhat lower yield suggests that there may be appreciably more of the isomeric product formed here. No data are available on the effects of a methyl group, unfortunately, since all efforts to convert the sodium sulfonate prepared from propylene oxide to an identifiable derivative were uniformly unsuccessful. Phenoxymethyl appears to be as strongly directive as phenyl, but in the opposite sense, since addition to phenyl glycidyl ether gave only the primary sulfonate, sodium 3-phenoxy-2-hydroxypropane sulfonate, in high yield.

TABLE III

THE EFFECT OF pH ON THE ADDITION OF SULFUROUS ACID SALTS TO STYRENE OXIDE^a

SO ₂ salts in solution ^b	Initial pH	Final pH	Time, hours	SO ₂ converted to addition product, %
NaHSO ₃	4.35	4.4	6	11
NaHSO ₃ (75%)	5.7	6.1	6	38
Na ₂ SO ₃ (25%)				
NaHSO ₃ (60%)	6.15	>13	6	74
Na ₂ SO ₃ (40%)				
NaHSO ₃ (50%)	6.35	>13	6	81
Na ₂ SO ₃ (50%)				
Na ₂ SO ₃	8.8	>13	6	87

^a Oxygen absent. ^b The total initial concentration of sulfurous acid salts in solution was approximately one molar in all cases. Where both bisulfite and sulfite were present, mole percentages are given.

While these results are self-consistent, their relationship to previously-reported work is not obvious. For that matter, the present state of the theory of base-catalyzed additions to unsymmetrical epoxides is one of chaos, the same substituent group being variously described by different authors (and even by the same author at different times) as "electron-attracting" and "electron-repelling," and no less than three distinct influences—polarization, steric interference and allylic resonance—having been postulated to explain discordances in orientation. Since it will be necessary to introduce still a fourth, the magnitude of the ionic charge, to correlate the whole, a certain amount of review is called for.

Simple aliphatic alcohols¹⁰ and phenol¹¹ add to propylene oxide to give secondary alcohol-primary ethers. The reaction of methanol with 3,4-epoxybutene-1 leads to a similar product.^{12,13} Addition

of methanol to styrene oxide, however, gives a mixture containing approximately one-third of the isomeric primary alcohol-secondary ether.¹⁴ Two factors are operative here: the negative alkoxide ion tends to attack the relatively positive substituted epoxide carbon position, but the polarization induced by the feebly electronegative (in the sense of Kharasch¹⁵) methyl and vinyl groups is outweighed by even mild steric repulsions, and the entering anion is directed to the terminal carbon. The phenyl substituent in styrene oxide, on the other hand, is strongly electronegative; the carbon atom to which it is attached thus becomes sufficiently positive to overcome the steric effect to a large extent. Addition of allyl alcohol yields a secondary alcohol-primary ether only with propylene oxide; with either styrene oxide or 3,4-epoxybutene-1 the product is exclusively the primary alcohol-secondary ether.¹⁶ Since alkoxide ion is a stronger base, in the Lewis sense, than methoxide ion, it may be concluded that even the lesser electronegativity of the vinyl group is sufficient to direct it to the secondary carbon atom. Sodionalonic¹⁷ and sodioacetoacetic esters¹⁸ should be comparable in the ring-opening addition to sodium alkoxide; the fact that they give the same secondary alcohol type of structure with styrene oxide as with propylene oxide must be attributed to the greatly increased steric interference. Confirmation of this view is found in the fact that with 3,4-epoxybutene-1 they yield about equal parts of primary and secondary alcohol, which indicates that the lesser inductive effect of the vinyl group is more than compensated for by its smaller bulk compared to phenyl. A tentative rating of the hydroxymethyl group as a relatively electropositive substituent may be made from the observation of Swern, Billen and Knight¹⁶ that the addition of sodium alkoxide to glycidol gives a mixture in which the primary ether predominates by a ratio of 2:1.

Sulfite ion is a weaker base than methoxide ion, and is if anything somewhat bulkier. Both factors should tend to favor attack at the terminal carbon atom with the formation of primary sulfonic acids. That only secondary sulfonates have been found, in the addition to octene oxide as well as styrene oxide, implies an additional factor not encountered in the studies quoted, one capable of outweighing both the weak polarization in octene oxide and the steric effect of the phenyl and hexyl groups. It is suggested that this lies in the divalent character of the sulfite ion; the double negative charge should be much more strongly attracted by an induced positive center than any of the monovalent anions cited. It appears, furthermore, from the fact that only primary sulfonates are formed by addition to phenyl glycidyl ether, that the phenoxymethyl group is at least as much more electropositive than hydrogen as *n*-hexyl is more negative, since if it were of intermediate strength the product should be a mixture of isomers.

(14) W. Reeve and I. Christoffel, *ibid.*, **72**, 1480 (1950).

(15) M. S. Kharasch and A. L. Flenner, *ibid.*, **54**, 674 (1932).

(16) D. Swern, G. N. Billen and H. B. Knight, *ibid.*, **71**, 1152 (1949).

(17) R. R. Russell and C. A. VanderWerf, *ibid.*, **69**, 11 (1947).

(18) R. M. Adams and C. A. VanderWerf, *ibid.*, **72**, 4368 (1950).

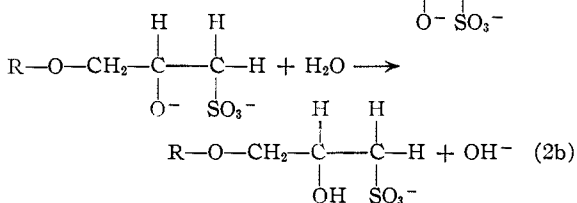
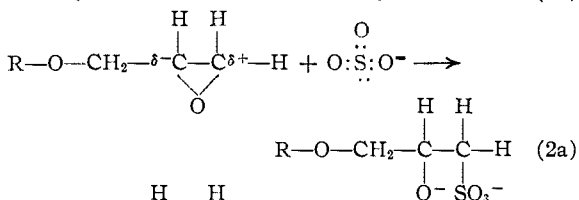
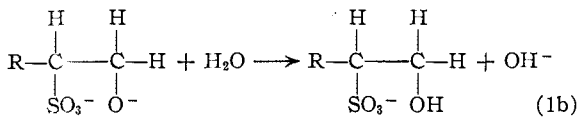
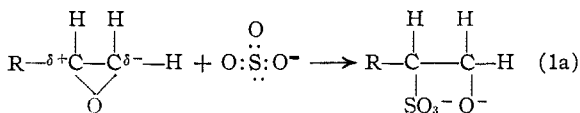
(10) H. C. Chitwood and B. T. Freure, *THIS JOURNAL*, **68**, 680 (1946).

(11) A. R. Sexton and R. C. Britton, *ibid.*, **70**, 3606 (1948).

(12) R. G. Kadesch, *ibid.*, **68**, 41 (1946).

(13) P. D. Bartlett and S. D. Ross, *ibid.*, **70**, 926 (1948).

The suggested mechanisms for the two antipodal modes of addition of sulfite ion to the oxirane ring may be diagrammed thus



The first step in each case is a displacement of the bridge oxygen by the nucleophilic sulfite ion, away from the more electron-deficient of the ring carbon atoms. This is followed by stabilization of the intermediate through reaction with water, to give a sulfonate ion and hydroxyl ion. In the presence of an excess of bisulfite, sulfite ion is then regenerated by reaction of bisulfite and hydroxyl ions.

The failure of bisulfite to add directly to the oxirane system may perhaps be explained by reference to the structure of sulfurous acid. It has often been suggested that sulfurous acid is asymmetrical, *i.e.*, one of the hydrogen atoms is linked to an oxygen atom and the other is bonded directly to the sulfur atom.¹⁹ Since there are here no unshared

electrons on the sulfur atom, the formation of a carbon-sulfur bond by the proposed mechanism would be unlikely. The inability of bisulfite ion to add to epoxides could therefore be construed as evidence in favor of an asymmetrical structure for sulfurous acid.

A study of the kinetics of the addition reaction was undertaken in an attempt to obtain additional evidence for the above mechanism. Sodium sulfite in one molar solution was shaken with a two-fold excess of styrene oxide and samples were analyzed at intervals. When the logarithm of the concentration of sodium sulfite remaining was plotted against time (Fig. 1), a straight line resulted. The reaction is therefore first order, and, since the concentration of the epoxide in the aqueous phase was constant as a result of its low solubility in water, it must be concluded that the rate of addition is proportional to the concentration of sulfite ion in solution. The reaction rate constant was calculated to be $9 \times 10^{-5} \text{ sec.}^{-1}$ at 25° .

A similar run was carried out in which a solution of sodium bisulfite was used in place of the sodium sulfite and the curve obtained when concentration of sulfurous acid salts was plotted against time is shown in Fig. 2. Except for a small irregularity at the beginning of the reaction, the plot is a straight line. This indicates a zero-order reaction, *i.e.*, the concentrations of all reacting species are constant. Since the concentration of bisulfite ion in solution was steadily decreasing, the actual reactant must have been the sodium sulfite which is present in small amounts in most commercial samples of sodium metabisulfite. This concentration of sulfite ion would remain essentially constant, since, as pointed out previously, it is regenerated as rapidly as it is consumed.

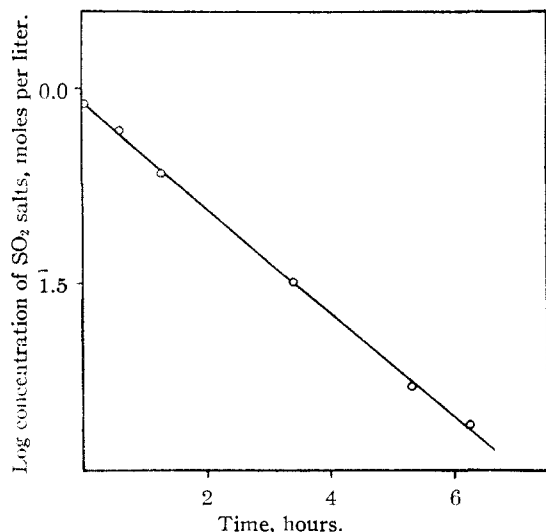


Fig. 1.—The rate of addition of sodium sulfite to styrene oxide.

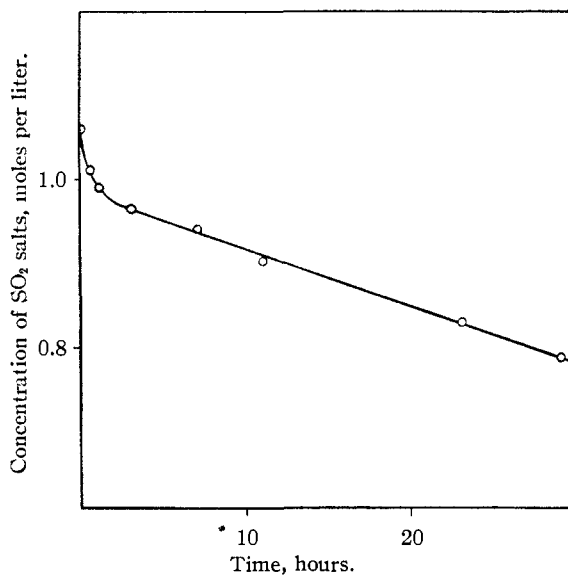


Fig. 2.—The rate of addition of sodium bisulfite to styrene oxide.

The concentration of sulfite ion in the one molar sodium bisulfite solution was calculated, by substituting the value of the slope of the linear portion of Fig. 2 into the equation for the rate constant for the addition of sulfite to styrene oxide, to be approx-

(19) J. W. Mellor, "A Comprehensive Treatise on Inorganic and Theoretical Chemistry," Vol. X, Longmans, Green and Co., New York, N. Y., 1930, pp. 234-241.

imately 0.021 molar. This corresponds to a concentration of approximately 2.7% by weight of sodium sulfite in the solid sodium metabisulfite. Analysis of the metabisulfite, by titration with standard HCl, showed that it contained between 2 and 3% of sodium sulfite. That this agreement was not fortuitous was established in the following manner.

Sulfurous acid was added to a sodium bisulfite solution in slight excess over the amount calculated to convert the sulfite present to bisulfite. The solution was then shaken with styrene oxide and the curve obtained by plotting concentration of sulfurous acid salts *vs.* time was again, except for the initial irregularity, a straight line. It was in this case, however, practically parallel to the horizontal axis. Only a minute amount of the addition product could be isolated.

Sodium sulfite was added to a one molar bisulfite solution in an amount calculated to double the concentration of sulfite ion already present. The plot of concentration of sulfurous acid salts *vs.* time was a straight line with a slope approximately twice that of Fig. 2.

An attempt was made to determine the reason for the initial irregularities in the reaction rate curves obtained when styrene oxide was treated with sodium bisulfite. These consisted of a comparatively rapid disappearance of sulfurous acid salts for a period of 1.5–2 hours. That this behavior was not due to any reactive impurity in either the styrene oxide or the bisulfite was shown by shaking a sample of the oxide with bisulfite solution for three hours, separating the phases, and then treating the oxide layer with fresh bisulfite and the original bisulfite with fresh oxide. Both these mixtures exhibited the same rapid initial consumption of sulfurous acid salts before levelling off once more. The product of this initial rapid reaction would not be a hydroxy sulfonate, since no more addition product could be isolated than could be accounted for by the linear portion of the reaction rate curve. Nor could the amount of sulfurous acid salts represented by the irregularity have been destroyed by autoxidation, since the air above the reaction mixture was always replaced by nitrogen, and even if this had not been done, the total amount of oxygen which could have been present would be equivalent to only about one-seventh of the sulfur dioxide consumed. The possibility remains that sulfur dioxide may also be consumed by an entirely independent rapid reaction catalyzed by traces of oxygen. This seems unlikely in view of the observation that the magnitude and shape of the kink in the curve was not affected by fairly large variations in the amount and concentration of the oxygen available. It is also hard to imagine what might have become of this sulfur dioxide, since it does not appear in the organic products.

The reaction rate curves for the addition of sulfite to phenyl glycidyl ether were similar to those obtained for styrene oxide, *i.e.*, the reaction is first order for the addition of sulfite. The reaction rate constant was calculated to be 5×10^{-6} sec.⁻¹ at 25°. The only isolatable addition product was proven to be sodium 3-phenoxy-2-hydroxypropanesulfonate.

Propylene oxide was selected as another representative epoxide to determine what effect a homogeneous system would have on the reaction. A twenty-fold excess of the epoxide was used in these runs, in order that its concentration should not be significantly altered during the course of the reaction. As anticipated, the addition of sulfite to propylene oxide was very much faster than to either styrene oxide or phenyl glycidyl ether. The rate could not conveniently be measured, as the reaction was complete within five minutes. In sodium bisulfite solution the addition was much slower. Plotting concentration of sulfurous acid salts against time again resulted in a straight line, indicating that the concentrations of all reactants were constant, *i.e.*, that bisulfite as such has no part in the addition reaction. The addition product could not be identified, since it was not found possible to isolate a suitable derivative.

1,2-Epoxyoctane exhibited only quantitative deviation from the behavior of the other three epoxides studied. Sulfite added very slowly, and the reaction with sodium bisulfite was too sluggish to be detectable. Reaction rate curves for the addition of sulfite showed the reaction to be first order, with a rate constant of 2×10^{-6} sec.⁻¹ at 25°. The addition product was identified as sodium 1-hydroxyoctane-2-sulfonate.

A recent article by Searles²⁰ reports the addition of bisulfite to trimethylene oxide. No reaction was observed in potassium bisulfite solution unless the pH had been lowered by saturation with sulfur dioxide. The product is said to be potassium 3-hydroxypropane sulfonate, though no evidence for this conclusion is offered except an analysis for potassium which is nearly 1% higher than the calculated. These results differ much more widely from those described above than is acceptable for systems as similar as oxirane and oxetane; the behavior of trimethylene oxide with salts of sulfurous acid has consequently been reinvestigated.

Searles' procedure for the reaction of acidified potassium bisulfite and trimethylene oxide, and for the isolation of the product, was duplicated. The product was shown to consist largely of the bisulfite addition compound of propionaldehyde, and to contain a considerable amount of inorganic potassium salts. The latter was probably responsible for the high potassium analysis. Formation of the aldehyde-bisulfite addition compound presumably results from an acid-catalyzed rearrangement of the trimethylene oxide to propionaldehyde.

Sodium sulfite also was found to add readily to trimethylene oxide, as demonstrated by the relatively rapid decrease in the amount of titratable sulfur dioxide in the solution. Although the structure of the product has not been proven, the fact that the pH of the mixture increases steadily with the progress of the addition to a value in excess of 13 indicates that the reaction is closely comparable to that undergone by the epoxides. The resulting salt is thus probably under these circumstances the 3-hydroxypropanesulfonate.

Experimental

Materials.—Baker and Adamson reagent grade sodium
(20) S. Searles, *THIS JOURNAL*, **73**, 4515 (1951).

metabisulfite and Merck reagent grade sodium sulfite were used.

Styrene oxide was supplied by the Dow Chemical Company. It was found to contain about 5% of an easily reducible impurity, presumably phenylacetaldehyde, which could not be removed by distillation. Purification was accomplished by treatment with hydrogen under a pressure of 3 atmospheres in the presence of platinum oxide; the epoxide is not reduced under these conditions, but the aldehyde is reduced to β -phenylethanol, from which the epoxide is readily fractionated. The product was collected at 84–86° (16.5 mm.).

Propylene oxide was obtained through the courtesy of the Carbon and Carbide Chemicals Corporation. It was used as received.

Phenyl glycidyl ether was prepared according to the method of Boyd and Marle.²¹ It was distilled through a 50-cm. packed column at 98–99° (4.5 mm.). The yield was 22.5%.

1,2-Epoxyoctane was prepared by the method of Swern, Billen and Scanlan.²² The product was distilled through a 40-cm. Vigreux column at 62–63° (17 mm.). The yield was 32%.

Trimethylene oxide was prepared according to Searles' modification²³ of the method of Derick and Bissell.²⁴ The product was distilled through a 50-cm. packed column at 48.5–49.5° (760 mm.). The yield was 25%.

The trimethylene chlorohydrin acetate from which trimethylene oxide was made was prepared by heating a mixture of 99 g. of trimethylene chlorohydrin (1.95 moles), 112 g. of acetic anhydride (1.10 moles) and 1 g. of *p*-toluenesulfonic acid hydrate on the steam-bath for 1 hr. After cooling to room temperature, the solution was poured into 1 l. of cold water. The layers were separated and the product washed with successive portions of water, 5% sodium bicarbonate solution and water. The yield of crude, dried over anhydrous magnesium sulfate, was 128 g. This was used without further purification.

General Procedure.—To determine whether the addition involved free radicals, the solutions were shaken in a 300-ml. Kjeldahl flask, fitted with a rubber stopper containing an inlet tube, which was connected to a graduated reservoir of pure oxygen collected over water. The atmosphere in the reaction flask was air, the oxygen concentration being kept constant by automatic replacement from the reservoir as it was consumed. The over-all pressure was maintained at 1 atmosphere. A reaction was carried out by measuring a quantity of a molar aqueous solution of sulfurous acid salts of the desired pH into the flask, and adding about two moles of epoxide per mole of sulfurous acid salts. The mixture was shaken until the concentration of sulfurous acid salts no longer diminished: 3 to 6 hours in most cases. Oxygen was absorbed quite rapidly as shaking was started, but the rate fell off as the reaction progressed and was usually very slow after the first few hours.

Where nitrite was used as the promoter, the air was displaced from the flask by a rapid stream of nitrogen. One-twentieth of a mole of sodium nitrite per mole of sulfurous acid salts was added to the reaction mixture, and the flask was then tightly stoppered and shaken.

Reactions under vacuum were carried out in an apparatus consisting of a yoke to which were sealed two cylindrical glass bulbs with side-arms, one of 50 ml. and the other of 20-ml. capacity. The yoke was connected to the high-vacuum line through a stopcock and was constricted near the larger bulb to permit sealing off while evacuated. Twenty-five ml. of molar bisulfite solution or of molar bisulfite-sulfite buffer of desired pH was introduced into the larger bulb through its side-arm and a twofold excess of epoxide was measured into the smaller. When the presence of anti-oxidants was in order, hydroquinone or *t*-butylcatechol was added to the bulb containing the aqueous solution. The side-arms were sealed off, the system evacuated and the solutions twice degassed. After the contents of the bulbs had come to room temperature, the epoxide was distilled over into the larger bulb. This was sealed off at the con-

striction, shaken for several hours, broken open and the contents analyzed.

Reaction rate measurements were carried out by shaking a number of identical samples of the desired bisulfite-sulfite solution with an approximately twofold excess of epoxide, and analyzing them singly at intervals. These reactions were conducted in 150 × 18 mm. test-tubes, filled with nitrogen, and each containing 10 ml. of salt solution and the appropriate quantity of epoxide. After addition had progressed for the proper length of time, a tube was withdrawn and to it was added 10 ml. of a 1:1 mixture of ether and ligroin to effect a rapid separation of epoxide and aqueous solution. Samples for analysis were pipetted from beneath the organic layer.

Sulfurous acid salts were estimated iodimetrically. Since varying amounts of aldehyde-bisulfite addition compounds were formed as by-products in some of the addition reactions, and since these compounds cannot conveniently be directly titrated with iodine because of their slow rate of decomposition in faintly acid solution, the following procedure was used to determine the total of sulfurous acid salts which neither added to the epoxide to form a stable addition compound nor were oxidized to sulfuric acid salts. A sample of the solution to be analyzed was added to an excess of standard iodine solution, followed by sodium bicarbonate to bring the pH of the mixture to approximately 7. At this acidity the decomposition of any aldehyde-bisulfite compound which may have been present was facilitated without interfering with the oxidation of bisulfite by iodine. After the solution had stood for several minutes the excess iodine was back-titrated with standard thiosulfate.

Isolation of Addition Product.—Excess epoxide was separated from the completed reaction mixture by extraction with ether. The salt solution was acidified to pH 1.5–2 with sulfuric acid and boiled until no more sulfur dioxide was evolved, then was neutralized with sodium hydroxide.²⁵ Thus sodium sulfate, which is practically insoluble in aqueous alcohol, was the only inorganic salt remaining. The solution was evaporated to dryness and any glycol, produced by hydration of the epoxide, was removed by triturating the residue with ether. The remaining mixed solids were extracted with boiling 80% alcohol; sulfonate crystallized from the extract on cooling.

Identification of Styrene Oxide Adduct.—One hundred ml. of 1 M sodium sulfite solution was shaken with excess epoxide, in the absence of oxygen, for 16 hr. At the end of this time, 94.5% of the starting sulfite had disappeared. The product was isolated by the procedure outlined above. Recrystallization from 70% alcohol afforded 20.4 g. of small white plates, which were dried at 110°. This corresponds to a conversion of 91% of the sulfite taken, or 96.4% of that which disappeared.

Anal. Calcd. for C₈H₈SO₄Na: Na, 10.26. Found: Na, 10.33.

The S-benzylisothiuronium salt was prepared by adding a solution of 1 g. of S-benzylisothiuronium chloride in 2 ml. of water to a solution of 1 g. of the sodium salt in 3 ml. of water. The product crystallized on cooling in ice-water. After recrystallization from water it melted at 124–125°.

Anal. Calcd. for C₁₅H₂₀O₄N₂S₂: N, 7.61. Found: N, 7.72.

Authentic Sodium 1-Phenyl-2-hydroxyethanesulfonate.—This was prepared by a procedure based on that of Hemelian.²⁶ Fifty ml. of a molar solution of ammonium sulfite was shaken for 20 hr. with a solution of 6 g. of 2-phenyl-2-iodoethanol in 50 ml. of ether.²⁷ The separated aqueous layer was freed from ammonia and unreacted sulfur dioxide and the product isolated as the sodium salt as described. The salt was recrystallized from 70% alcohol and dried at 110°.

Anal. Calcd. for C₈H₈SO₄Na: Na, 10.26. Found: Na, 10.33.

(25) If sodium nitrite had been used as oxidant in the reaction, 1.1 moles of sodium carbonate per mole of nitrogen present was first added to the original aqueous solution and the mixture boiled until no more ammonia could be detected. Sulfur dioxide was then eliminated by the procedure described.

(26) W. Hemelian, *Ann.*, **168**, 146 (1873).

(27) Substitution of ammonium for sodium sulfite in replacement reactions is calculated to maintain the pH at neutrality, or slightly on the acid side. Loss of the orientation of the starting material through epoxide formation is thus minimized.

(21) D. R. Boyd and E. R. Marle, *J. Chem. Soc.*, **93**, 840 (1908).

(22) D. Swern, G. N. Billen and J. T. Scanlan, *THIS JOURNAL*, **68**, 1504 (1946).

(23) S. Searles, *ibid.*, **73**, 124 (1951).

(24) C. G. Derick and D. W. Bissell, *ibid.*, **38**, 2478 (1916).

2-Phenyl-2-iodoethanol.—The method by which this compound was prepared was based on that of Tiffeneau.²⁸ Hydrogen iodide was bubbled through a suspension of 15 g. of styrene oxide in 100 ml. of water, the mixture being cooled in ice throughout the addition. The oil gradually coagulated to a curdy, yellowish solid, which was recrystallized from alcohol; m.p. 78–79°. It decomposed slowly on standing and was therefore used at once.

The S-benzylisothiuronium salt of authentic sodium 1-phenyl-2-hydroxyethanesulfonate was prepared by mixing concentrated aqueous solutions of 1 g. of the reagent and 1 g. of the sulfonate. It was recrystallized from water; m.p. 124–125°. A mixture of this with the corresponding salt prepared from the styrene oxide adduct showed no depression in melting point.

Anal. Calcd. for C₁₆H₂₀O₄N₂S₂: N, 7.68. Found: N, 7.78.

Authentic Sodium 2-Phenyl-2-hydroxyethanesulfonate.—This was prepared by the addition of sodium bisulfite to styrene, according to the method of Kharasch, Schenck and Mayo.⁹ The S-benzylisothiuronium salt melted at 148.5–149.5°. When this derivative was mixed with that obtained from the styrene oxide adduct the combination melted over a wide range, starting at about 115°.

Propylene Oxide Addition Product.—This adduct was isolated in the same manner as that of styrene oxide. It crystallized from 80% alcohol as white plates and was dried *in vacuo* over phosphorus pentoxide.

Anal. Calcd. for C₃H₇SO₄Na: Na, 14.20. Found: Na, 14.08.

Both the possible isomers were synthesized for comparison, but since no suitable derivative of any of the three could be prepared, it was not possible to establish the structure of the adduct.

Identification of Phenyl Glycidyl Ether Adduct.—One hundred ml. of 1 M sodium sulfite solution was shaken with excess epoxide, in the absence of oxygen, for 20 hr. At the end of this time, 73% of the starting sulfite had disappeared. The product was isolated by the usual method, and on recrystallization from alcohol was obtained as 17.5 g. of pearly white plates, which were dried *in vacuo* over phosphorus pentoxide. This is a yield of 69% of the sulfite taken, or 94.5% of that consumed.

Anal. Calcd. for C₉H₁₁SO₃Na: Na, 9.05. Found: Na, 8.98.

The S-benzylisothiuronium salt prepared from the above adduct melted at 125.5–127°.

Anal. Calcd. for C₁₇H₂₂O₅N₂S₂: N, 7.04. Found: N, 6.89.

Authentic Sodium 3-Phenoxy-2-hydroxypropanesulfonate.—The method of preparation was modeled after that of Houlton and Tartar.²⁹ Five grams of 3-phenoxy-1-chloropropanol-2 was refluxed for 10 hr. with a solution of 5 g. of sodium sulfite in 25 ml. of water. The product was isolated in the standard manner, recrystallized from 70% alcohol and dried over phosphorus pentoxide *in vacuo*.

Anal. Calcd. for C₉H₁₁SO₃Na: Na, 9.05. Found: Na, 9.08.

3-Phenoxy-1-chloropropanol-2.—This compound was prepared according to the method of von Lindemann³⁰ from phenol and epichlorohydrin. The product was obtained as a yellowish oil, of b.p. 120–124° (3 mm.), in a yield of 8.5%.

The melting point of the S-benzylisothiuronium salt of authentic 3-phenoxy-2-hydroxypropanesulfonate was found to be 125.5–126.5°. In admixture with the corresponding salt of the phenyl glycidyl ether adduct the melting point was unchanged.

Anal. Calcd. for C₁₇H₂₂O₅N₂S₂: N, 7.04. Found: N, 7.12.

(28) M. Tiffeneau, *Ann. chim.*, [8] **10**, 348 (1907).

(29) H. G. Houlton and H. V. Tartar, *This Journal*, **60**, 544 (1938).

(30) Th. von Lindemann, *Ber.*, **24**, 2146 (1891).

Authentic Sodium 3-Phenoxy-1-hydroxypropane-2-sulfonate.—This was prepared from 3-phenoxy-2-chloropropanol-1 by the method given for the isomeric substance above.

Anal. Calcd. for C₉H₁₁SO₃Na: Na, 9.05. Found: Na, 9.21.

3-Phenoxy-2-chloropropanol-1.—Forty-five grams of phenyl allyl ether was added to 900 ml. of a 4% solution of HOCl prepared by the method of Wohl,³¹ and the mixture stirred at 0° for 8 hr. The organic layer was then separated and distilled. There was obtained 11 g. (17.8%) of product as a viscous, yellowish oil boiling at 118–122° (4.5 mm.).

The S-benzylisothiuronium salt of authentic 3-phenoxy-1-hydroxypropane-2-sulfonate was found to melt at 122–124°. When this was mixed with that obtained from the phenyl glycidyl ether adduct the melting point was markedly depressed.

Identification of 1,2-Epoxyoctane Adduct.—One hundred ml. of 1 M sodium sulfite solution was shaken with excess epoxide, in the absence of oxygen, for 62 hr. At the end of this time, 17% of the starting sulfite had been consumed. The product was isolated as usual, and was obtained, by recrystallization from 70% alcohol, as 3.4 g. of small white plates of considerably lower water solubility than the other analogous sulfonates. The conversion was thus 14.5% of the sulfite taken and 85.3% of that disappeared.

Anal. Calcd. for C₈H₁₇SO₄Na: Na, 9.91. Found: Na, 10.10.

The S-benzylisothiuronium salt of the above octene oxide addition product melted at 98.5–100°.

Anal. Calcd. for C₁₆H₂₈O₄N₂S₂: N, 7.45. Found: N, 7.31.

Authentic Sodium 2-Hydroxyoctane-1-sulfonate.—This was prepared by the method of Houlton and Tartar²⁹ from 1-chlorooctanol-2 and sodium sulfite. The product was recrystallized from 70% alcohol.

Anal. Calcd. for C₈H₁₇SO₄Na: Na, 9.91. Found: Na, 10.03.

The S-benzylisothiuronium salt of the authentic primary sulfonate immediately above melted at 108–110°. The melting point of a mixture with the derivative of the octene oxide addition product showed a decided depression. The latter is therefore presumably, like the product from styrene oxide, the secondary sulfonate-primary alcohol.

1-Chlorooctanol-2.—The addition of HOCl to 1-octene, by the same technique as outlined for phenyl allyl ether, produced 1-chlorooctanol-2 boiling at 108–112° (17 mm.). The yield from 50 g. of octene was 16 g., or 28%.

Additions to Trimethylene Oxide.—The procedure of Searles²⁰ was duplicated. Analysis of the salt obtained on evaporation of the alcoholic soxhlet extract showed it to contain 25.7% of potassium; since the potassium content of a potassium hydroxypropane sulfonate is 22.4%, there must have been present a fairly high proportion of inorganic potassium salts. On titration of this salt mixture with standard iodine, a 0.228-g. sample consumed 20.3 ml. of 0.106 N solution. This is equivalent to 30.2% sulfur dioxide in the sample. Assuming the inorganic potassium salt content indicated by the high ash determination to be entirely potassium metabisulfite, only 15.0% available sulfur dioxide can be accounted for. The balance of 15.2% sulfur dioxide would correspond to a content of 38.5% of aldehyde-bisulfite compound. One gram of the salt mixture was heated with 5 ml. of a 10% sodium carbonate solution and the effluent vapors were passed into 30 ml. of saturated aqueous dimedone. A crystalline precipitate slowly formed in the solution. The melting point of this product was found to be 152–153.5°, unaffected by admixture with a corresponding derivative prepared from known propionaldehyde.

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(31) A. Wohl, *ibid.*, **40**, 94 (1907).